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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,521	03/01/2005	Markus Hecker	DEBE:054US	9672

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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,521	HECKER ET AL.	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) *3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 March 2005* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-08-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of claims. Claims 1-3 are pending. Applicant's election **with traverse** of Group I drawn to claims I and 2 in the reply filed on 06-11-2007 is acknowledged.

With regard to restriction requirements, Applicant of election of SEQ ID NO: 15 for examination is acknowledged.

Response to arguments

On page 2 of Applicant's Response to the Restriction Requirements, Applicant argues that the examiner by objecting the unity of the invention does not fully understand the invention because the so-called "decoys" are never translated but serve as double-stranded DNA, which provide a sequence, to which a transcription factor binds in the cell and thus serve for the competitive inhibition of said transcription factors.

The examiner appreciates the correction about the fact that the double-strand DNA molecules are introduced into a cell with the intended used of binding transcription factors to serve as competitive inhibitors of said transcription factor. However, the examiner has established on page 3, last paragraph, bridging to page 4, paragraph 1, that the inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same corresponding technical feature as different transcription factors in addition to AP-1 have been described that have no substantial common core structures one from the others (e.g., TFIIA, E2F, Oct-4, Sox 2) and regulate different diseases. In other words, transcription factors bind specific positions in the promoter domain of a target gene and thus activate transcription of said gene regulating different physiological processes. Moreover, DNA fragments containing specific binding positions for transcription

factors have also been described as competitive inhibitors of said transcription factors to the endogenous target sequence.

On page 2 of applicant's remarks, applicant argues that "the 9-mer core-binding sequence are key nucleotide residues of the decoy that facilitate binding of any AP1 transcription factor. Thus, the Markush group of sequences satisfies the requirements of functional and structural homology, and as such, restriction is improper". Moreover, Applicant cites the M.P.E.P. at § 803.02 to support that the restriction requirements does not meet the Patent Office requirements because (i) the number of members of the Markush group **share a common utility** and (2) **share a substantial structural feature essential to that utility. Such is not persuasive.**

The examiner has required restriction among independent inventions with distinct functional domains drawn to different chemical structures, physical properties, and biological functions as a result of containing different genes sequences, which required separate searches for the following reasons. The target of all the oligonucleotides of SEQ ID NO: 1-36, as recited in claim 3, is the same transcription factor AP-1 and their sequences resembles the natural AP-1 core binding sequence in the genome (Specification, page 10, lines 15-16). However, each one of the disclosed sequences have distinct structure and functionally as evidence by the numerous examples in the as-filed specification. For example, Figures 1 and 2 teach neutralization of the transcription factor AP-1 and significantly reduced expression of CD40 receptor protein in endothelial cells after incubation with AP-1 decoy oligonucleotides of SEQ ID No. 3, 5, 11, 13, and 35 in relation to control oligonucleotides (page 12, lines 5-15). Additionally, as detected by Western- Blot the level of expression of CD40 is directly correlated to the sequence of the AP-1 decoy used for the competitive inhibition of AP-1. These results evidence that the sequences

claimed do not share a substantial structural feature. As such, not only a prior art search has to be conducted for each of the species, a prior art consideration and/or examination of arts relevant to the claimed invention as a whole would be unduly burdensome to the examiner. The examiner also notices that the biological sequence databases required to be searched for the examination of any biological sequence have grown tremendously, and thus the Technology Center no longer routinely examines and searches more than one independent biological sequence for any single application.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3 are pending in the instant application. Of these, claim 3 is withdrawn from consideration pursuant to 37 CFR1.14(b) as being drawn to nonelected invention, there being no allowable generic or linking claim.

Claims 1 and 2 are currently under examination to which the following grounds of rejection are applicable

Priority

Filing of a certified non-translated copy of the foreign application, DE 10240417.8 is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office. The information disclosure statement filed on 11-08-2005 fails to comply with 37 C.F.R. 1.98(a)(2), which requires a legible copy of each U.S. and

foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The information disclosure statement filed on 11-08-2005 has been considered for foreign documents DE10059144 and JP2001095573A to the extend that an English translated abstract is provided.

Specification objections

The Specification is objected because of the use of hyperlinks and other forms of browser-executable code. Specifically at page 12, line 31. 37 CFR 1.57(d) states that incorporation by reference by hyperlink or other form of browser executable code is not permitted. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See 37 CFR 1.57(d) and MPEP § 608.01(p)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under **35 USC**. 102(b) as being anticipated by Lillie et al., WO200151628-A2., Date of publication 19-July-2001 (see Result 17, on the attached search print out titled "Application 10/526521 and Search Result us-10-526-521-15.rng.").

Claims 1 and 2 are broadly interpreted, as any double-strand DNA oligonucleotide in a cell wherein one of the two DNA strands provides a sequence according to SEQ ID No. 15 and

the other strand is the complementary strand to SEQ ID No. 15.

Lillie et al., teach novel polynucleotides and fragments thereof, as markers for detecting, diagnosing, monitoring, and potentially preventing breast cancer. Specifically, Lillie et al., teaches a nucleotide molecule of 231 nucleotides (Claim 1; Page 97) comprising a nucleotide sequence having 100% homology with the double-strand oligonucleotide of SEQ ID No. 15 (see Result 17, on the attached search print out titled "Application 10/526521 and Search Result us-10-526-521-15.rng). Absent evidence to the contrary, the 231 nucleotide Sequence of Lillie et al., comprises regions of full identity to SEQ ID NO:15. Thus, the 231 nucleotide Sequence of Lillie et al., is a nucleotide sequence homologous to SEQ ID NO:15 having all the properties cited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cho-Chung (US Patent 6,060,310, Date of Publication May 9, 2000) in view of Morishita et al., (Diabetologia, 2001, pp. 713-720).

Claim 1 is directed to any double-strand DNA oligonucleotide wherein one of the two DNA strands provides a sequence according to SEQ ID No. 15 and the other strand is the complementary strand to SEQ ID No. 15. The as-filed specification teaches that the 13- base pair double stranded DNA of SEQ ID No. 15 is capable of binding in a sequence-specific manner to the transcription factor activator or activating protein-1 (AP-1) (p. 11, lines 1-3). SEQ ID No. 15 comprises a AP-1 consensus identical to the core binding sequence of AP-1 of SEQ ID No. 2, i.e., 5'-V**TGAGTCA**S-3' (page 11, line 9; page, 15, line 26; page 12, lines 9-12).

Cho-Chung teaches use of decoy oligonucleotides that competitively bind to transcription factors to inhibit gene expression. At column 23, lines 50-54, Cho-Chung teaches the transcription factor decoys regulate gene expression by being recognized and bound by transcription factors such that the factors can no longer bind to native response elements and regulate gene expression. The decoys can comprise one or more duplex nucleic acid structures recognized by the DNA binding domain of the target transcription factors, including decoys that comprise the consensus sequence for the targeted transcription factor (col. 10, lines 35-41). Cho-Chung exemplifies the invention with a decoy targeted to the consensus sequence of the cAMP

response element (col. 30, lines 35-37, Example 1). Moreover, Cho-Chung discloses that the invention is general and can target any transcription factor (col. 23, lines 50-67).

Cho-Chung et al., does not specifically teach decoys targeted to AP-1.

Hoverer, at the time the invention was made, Morishita et al. teach that regulation of AP-1 in *PAI-1* gene expression using a double-stranded cis-element AP-1 decoy. Morishita et al. teach at page 714, col. 2, paragraph 4, the generation of double stranded decoys against the AP-1 biding site used as competitive inhibitors of AP-1 and mismatched decoys as control molecules. Further, Morishita et al., teaches a 7-nucleotide consensus binding sequence for AP-1 i.e., 5'-AGCTTG**TGAGTCA**GAGCT-3'(underlined).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make duplex DNA decoy oligonucleotides comprising a consensus binding sequence of a transcription factor as taught by Cho-Chung and to make the decoy with the consensus sequence of AP-1 as taught by Morishita et al. Cho-Chung et al. provide a motivation to make duplex decoy oligonucleotides that bind a transcription factor by teaching such decoys are useful to inhibit gene expression through blocking action of the transcription factor and further provide a motivation to make a decoy comprising a consensus binding sequence by explicitly suggesting targeting of such a sequence and actually exemplifying use of such a sequence. Based on the combined teachings of Morishita et al, of the consensus binding sequence of AP-1, and the suggestion by Cho-Chung et al. to make decoy oligonucleotides targeted to consensus binding sequences, one of ordinary skill in the art would recognize a decoy of 13- base pair double stranded DNA of SEQ ID No. 15 that comprises the consensus binding sequence of AP-1 and the additional 3 flanking nucleotides to both the 5' and 3' site present in

the sequence shown as SEQ ID NO: 15 to be just one of many possible AP-1 decoys that would be produced in the course of routine optimization. One of ordinary skill in the art would have had a reasonable expectation of success in making a decoy oligonucleotide comprising the consensus sequence of AP-1 because Morishita et al. teach the sequence and because Cho-Chung actually exemplify synthesis of a decoy comprising a transcription factor consensus binding sequence.

Conclusion

Claims 1 and 2 are not allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also

enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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